In a paper the following year Palade (1953) offered a number of arguments for localizing the enzyme systems in the cristae. First, he noted that a number of experiments, such as those of Lehninger, indicated that a substrate has to penetrate inside the mitochondrion before it is acted upon. Second, he pointed out that particles comparable in size to individual cristae and containing most of the succinoxidase systems of the mitochondria had been isolated from suspensions of disintegrated mitochondria (see below). Finally, he suggested that if the enzyme systems were located in the cristae rather than the outer membrane, they would be less exposed and protected from disruption.

A Competing Perspective on Mitochondrial Morphology

Although the Rockefeller laboratory of Porter and Palade played the central role in developing the new conceptions of cell structure and function discussed so far, there were competing laboratories, especially in Europe, which challenged several of their claims. The most vocal opponent was Fritiof Stig Sjöstrand, who in the 1950s established a major electron microscopy laboratory at the Karolinska Institute in Stockholm. As a medical and doctoral student at the Karolinska during World War II, Sjöstrand had begun working with an electron microscope built by Manne Siegbahn, a physicist at the Royal Swedish Academy of Sciences. Based on his early attempts to develop thin sections he had published micrographs of muscle in *Nature* in 1943 that were suggestive but provided little detail (Sjöstrand, 1943). In September 1947, in a meeting with R. R. Struthers, he (unsuccessfully) appealed to the Rockefeller Foundation for an electron microscope, noting that the only functioning microscope in Stockholm was in the Department of Histology. Struthers noted in his diary that Sjöstrand "appears more than usually intelligent and diligent and makes an excellent impression."

Supported by a Swedish State Research Council Fellowship, Sjöstrand spent the 1947–8 academic year at MIT working with Francis Schmitt on

lately identified as mitochondria. It is known (Schneider & Hogeboom, '51) that this system is actually a mixture of cell debris, nuclei, and mitochondria, a fact that renders more difficult the interpretation of the results mentioned. What happens in a 'cyclophorase system' does not necessarily take place exclusively in mitochondria" (p. 437). For his part, Green credits the electron micrographs of Palade and Sjöstrand with providing "independent confirmation of the organization deduced from functional considerations. These microscope studies readily disposed of the then current hypothesis that all the enzymes and coenzymes of the mitochondria were present as freely diffusible molecular species without any special organization in the fluid interior of the mitochondrial 'bag,' which was surrounding by a semipermeable membrane" (Green, 1957–8, p. 178).